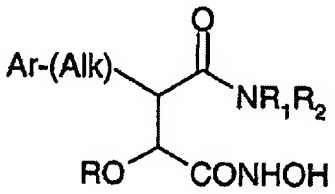
The listing of claims will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

1. (Currently Amended) A compound of formula (I), or an enantiomer or diastereoisomer thereof, or a salt, hydrate or solvate thereof:



(I)

wherein Ar represents an optionally substituted phenyl~~aryl, heteroaryl, C_3-C_8 cycloalkyl or heterocycloakyl group~~;

R represents hydrogen or C_1-C_6 alkyl, or C_3-C_6 cycloalkyl;

Alk represents a divalent C_1-C_5 alkylene or C_2-C_5 alkenylene radical; and

R_1 and R_2 taken together with the nitrogen atom to which they are attached form a piperazinyl ring ~~first heterocycloalkyl ring which is optionally fused to a second C_3-C_8 cycloalkyl or heterocycloalkyl ring, the said first and second rings being~~ optionally substituted by at least one group of formula (II):

(II)

wherein m, p and n are independently 0 or 1;

Z represents, hydrogen, or an optionally substituted carbocyclic or heterocyclic ring of from 5 to 7 ring atoms which is optionally fused to another optionally substituted carbocyclic or

heterocyclic ring of from 5 to 7 ring atoms;

Alk^1 and Alk^2 independently represent optionally substituted divalent C_1-C_3 alkylene radicals;

X represents -O-, -S-, -S(O)-, -$S(O_2)$-, -C(=O)-, -NH-, -NR_3-, -$S(O_2)$NH-, -$S(O_2)NR_3$-, -$NHS(O_2)$-, or -$NR_3S(O_2)$-, where R_3 is C_1-C_3 alkyl.

2. (Original) A compound as claimed in claim 1 wherein R is hydrogen.

3. (Original) A compound as claimed in claim 1 wherein R is methyl.

4. (Original) A compound as claimed in claim 1 wherein R is ethyl, n-propyl, isopropyl, n-, sec- or tert-butyl, cyclopropyl, or cyclopentyl.

5. (Currently Amended) A compound as claimed in Claim 1 wherein Ar is ~~a 5- or 6-membered monocyclic aryl or heteroaryl ring, which is optionally~~ substituted by at least one substituent selected from (C_1-C_3)alkyl, (C_1-C_3)alkoxy, hydroxy, hydroxy(C_1-C_3)alkyl, mercapto, mercapto(C_1-C_3)alkyl, (C_1-C_3)alkylthio, halo, trifluoromethyl, trifluoromethoxy, nitro, nitrile (-CN), -COOH, -$COOR^A$, -COR^A,-SO_2R^A, -$CONH_2$, -SO_2NH_2, -$CONHR^A$, -SO_2NHR^A, -$CONR^AR^B$, -$SO_2NR^AR^B$, -NH_2, -NHR^A, -NR^AR^B, -$OCONH_2$, -$OCONHR^A$, -$OCONR^AR^B$, -$NHCOR^A$, -$NHCOOR^A$, -NR^BCOOR^A, -$NHSO_20R^A$, -$NR^BSO_2OR^A$, -$NHCONH_2$, -NR^ACONH_2, -$NHCONHR^B$, -NR^ACONHR^B, $NHCONR^AR^B$, or -$NR^ACONR^AR^B$ wherein R^A and R^B are independently C_1-C_3 alkyl, phenyl or a 5- or 6-membered monocyclic aryl or heteroaryl ring.

6. (Currently Amended) A compound as claimed in claim 5 wherein the phenyl ring is ~~an optional substituent is~~ substituted in the 4- position ~~in the case of a 6-membered ring, or in the 2- and/or 3- position in the case of a 5-membered ring~~.

7. (Canceled)

8. (Previously Presented) A compound as claimed in Claim 1 wherein optional substituents

in Ar are selected from methoxy, ethoxy, trifluoromethoxy, methyl, ethyl, trifluoromethyl, hydroxyl, mercapto, fluoro, chloro, and bromo.

9. (Original) A compound as claimed in claim ~~5~~ 1 wherein Ar is 4-(C_1C_3alkoxy)phenyl.

10. (Previously Presented) A compound as claimed in claim ~~5~~ 1 wherein Ar is 4-ethoxyphenyl.

11. (Previously Presented) A compound as claimed in Claim 1 wherein Alk is $-CH_2-$, $-CH_2CH_2-$, $-CH_2CH(CH_3)-$, $-CH_2CH_2CH_2-$, $-CH_2CH_2CH_2CH_2-$, $-CH=CH-$, $-CH_2CH=CH-$, $-CH_2CH=CHCH_2-$, or $-CH=CHCH=CH-$.

12. (Canceled)

13. (Canceled)

14. (Previously Presented) A compound as claimed in Claim 1 wherein in the group (II), when present, p is 0, Z is hydrogen and at least one of n and m is 1.

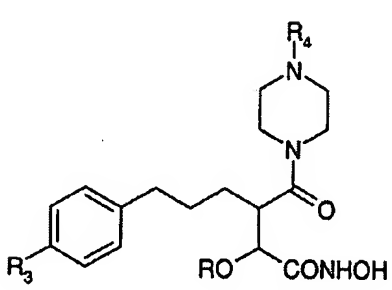
15. (Previously Presented) A compound as claimed in Claim 1 wherein in the group (II), when present, m, n and p are all 0 and Z is a carbocyclic or heterocyclic ring directly linked to a ring carbon or ring nitrogen of the $-NR_1R_2$ group.

16. (Previously Presented) A compound as claimed in Claim 1 wherein in the group (II), when present, p is 0, at least one of m and n is 1, and Z is a carbocyclic or heterocyclic ring linked to a ring carbon or ring nitrogen of the $-NR_1R_2$ group via a C_1-C_6 alkylene linker between Z and the $-NR_1R_2$ ring.

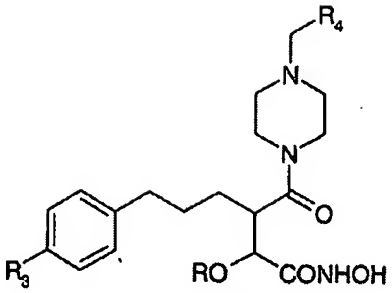
17. (Previously Presented) A compound as claimed in Claim 1 wherein in the group (II), when present, p is 1.

18. (Original) A compound as claimed in claim 1 of formula (1B) or (IC) or an enantiomer

or diastereoisomer thereof, or a salt, hydrate or solvate thereof:



(IB)

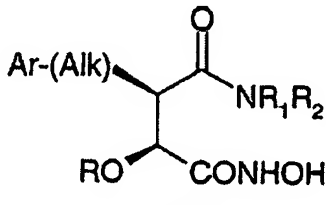


(IC)

wherein R is hydrogen or methoxy, R_3 is trifluoromethyl, trifluoromethoxy C_1-C_3 alkoxy, hydroxy, or halo; R_4 is (i) $-SO_2R_5$ or $-COR_5$ wherein R_5 is C_1-C_6 alkyl or phenyl or monocyclic heteroaryl having 5 or 6 ring atoms, optionally substituted by (C_1-C_3)alkyl, (C_1-C_3)alkoxy, hydroxy, hydroxy(C_1-C_3)alkyl, mercapto, mercapto(C_1-C_3)alkyl, (C_1-C_3)alkylthio, halo, trifluoromethyl, trifluoromethoxy or (ii) phenyl or monocyclic heteroaryl having 5 or 6 ring atoms; optionally substituted by (C_1-C_3)alkyl, (C_1-C_3)alkoxy, hydroxy, hydroxy(C_1-C_3)alkyl, mercapto, mercapto(C_1-C_3)alkyl, (C_1-C_3)alkylthio, halo, trifluoromethyl, trifluoromethoxy.

19. (Original) A compound as claimed in claim 18 wherein a heteroaryl ring forming part of R_4 is pyridyl, pyrimidinyl, triazinyl, thienyl, or furanyl.

20. (Previously Presented) A compound as claimed in Claim 1 having the stereochemical configuration shown in formula (IA):



(IA)

21. (Currently Amended) A compound as claimed in claim 1, which is selected from the group consisting of:

~~6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(pyrrolidine-1-carbonyl)-hexanoic acid hydroxyamide.;~~

~~3R-(6,7-dimethoxy-3,4-dihydro-1H-isoquinoline-2-carbonyl)-6-(4-ethoxyphenyl)-2S-hydroxy-hexanoic acid hydroxyamide.;~~

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(3-methoxy-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-methoxy-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-4-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide;

~~6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(morpholine-4-carbonyl)-hexanoic acid hydroxyamide.~~

~~6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(2RS-methyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide.;~~

~~6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(2,6-RS-dimethyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide.;~~

~~6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(thiomorpholine-4-carbonyl)-hexanoic acid hydroxyamide.;~~

~~3R-(4-benzyl-piperidine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;~~

3R-(4-benzo[1,3]dioxol-5-ylmethyl-piperazine-1-carbonyl)-6-(4-ethoxyphenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-4-ylmethyl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-benzylpiperazine-1-carbonyl)-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(4-pyrimidin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-trifluoromethyl-pyrimidin-2-yl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-chloro-pyrimidin-2-yl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;
3R-[4-(4,6-dimethoxy~[1,3,5]triazin-2-yl)-piperazine-1-carbonyl]-6-(4-ethoxyphenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(3-trifluoromethyl-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;
6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(2-fluoro-phenyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

~~3R-[4-(acetyl-methyl-amino)-piperidine-1-carbonyl]-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;~~

~~6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(methyl-propyl-amino)-piperidine-1carbonyl]-~~

~~hexanoic acid hydroxyamide.;~~

~~6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(3S-benzyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide.;~~

~~6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(3S-isobutyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide.;~~

~~6-(4-ethoxy-phenyl)-2S-hydroxy-3R-(3S-phenyl-morpholine-4-carbonyl)-hexanoic acid hydroxyamide.;~~

3R-(4-benzyl-3RS-methyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S hydroxy-hexanoic acid hydroxyamide.;

3R-(3S,4-dibenzyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxyhexanoic acid hydroxyamide.;

3R-(4-benzyl-3RS-phenyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide.;

4-(4-benzo[1, 3]dioxol-5-ylmethyl-piperazin-1-yl)-2S, N-dihydroxy-4-oxo-3R-(4-trifluoromethoxy-benzyl)-butyramide.;

~~3R-benzyl-2S, N-dihydroxy-4-morpholin-4-yl-4-oxo-butyramide.;~~

~~3R-(4-Benzyloxy-benzyl)-2S, N-dihydroxy-4-oxo-4-piperidin-1-yl-butyramide.;~~

~~2S, N-dihydroxy-3R-(4-hydroxy-benzyl)-4-oxo-4-piperidin-1-yl-butyramide.;~~

4-(4-benzo[1, 3]dioxol-5-ylmethyl-piperazin-1-yl)-3R-(4-benzyloxy-benzyl)2S, N-dihydroxy-4-oxo-butyramide;

~~6-(3, 5-bis-trifluoromethyl-phenyl)-2S-hydroxy-3R-(morpholine-4-carbonyl)hexanoic acid hydroxyamide;~~

~~3R-(4-benzyl-piperidine-1-carbonyl)-6-(3,5-bis-trifluoromethyl-phenyl)-2S-hydroxy-hexanoic acid hydroxyamid.;~~

6-(3, 5-bis-trifluoromethyl-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide;

~~6-(3, 5-bis-trifluoromethyl-phenyl)-3R-(6, 7-dimethoxy-3,4-dihydro-1 H-isoquinoline-2-carbonyl)-2S-hydroxy-hexanoic acid hydroxyamide;~~

~~6-(3, 5-bis-trifluoromethyl-phenyl)-2S-hydroxy-3R-(pyrrolidine-1-carbonyl)-hexanoic acid hydroxyamide~~

3R-(2S-benzyl-4-methyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyJ)-2Shydroxy-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-trifluoromethoxy-benzenesulfonyl)piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(toluene-4-sulfonyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

3R-[4-(5-bromo-thiophene-2-sulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxyphenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

3R-[4-(5-benzenesulfonyl-thiophene-2-sulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

3R-[4-(4-butoxy-benzenesulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxy-phenyl)2S-hydroxy-hexanoic acid hydroxyamide;

6-(4-ethoxy-phenyl)-2S-hydroxy-3R-[4-(4-methoxy-2,3, 6-trimethylbenzenesulfonyl)-piperazine-1-carbonyl]-hexanoic acid hydroxyamide;

3R-[4-(3,4-dimethoxy-benzenesulfonyl)-piperazine-1-carbonyl]-6-(4-ethoxyphenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

6-(4-methoxy-phenyl)-2S-hydroxy-3R-[4-(2-fluoro-phenyl)-piperazine-1carbonyl]-hexanoic acid hydroxyamide;

6-(4-methoxy-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide;

6-(4-fluoro-phenyl)-3R-[4-(2-fluoro-phenyl)-piperazine-1-carbonyl]-2S-hydroxy-hexanoic acid hydroxyamide;

6-(4-fluoro-phenyl)-2S-hydroxy-3R-(4-pyridin-2-yl-piperazine-1-carbonyl)-hexanoic acid hydroxyamide;

3R-(4-benzyl-2S-methyl-piperazine-1-carbonyl)-6-(4-ethoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

3R-(4-benzyl-2S-methyl-piperazine-1-carbonyl)-6-(4-methoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

3R-(4-benzyl-2S-i-butyl-piperazine-1-carbonyl)-6-(4-methoxy-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

3R-(4-benzyl-2S-methyl-piperazine-1-carbonyl)-6-(4-fluoro-phenyl)-2S-hydroxy-hexanoic acid hydroxyamide;

3R-(4-benzyl-2S-i-butyl-piperazine-1-carbonyl)-6-(4-fluoro-phenyl)-2S-hydroxy-hexanoic

acid hydroxyamide;

4-[5-(4-ethoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-methyl-piperazine-1-carboxylic acid tert-butyl ester;

4-[5-(4-ethoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-i-butyl-piperazine-1-carboxylic acid tert-butyl ester;

4-[5-(4-methoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-methyl-piperazine-1-carboxylic acid tert-butyl ester;

4-[5-(4-methoxy-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-i-butyl-piperazine-1-carboxylic acid tert-butyl ester;

4-[5-(4-fluoro-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-methyl-piperazine-1-carboxylic acid tert-butyl ester.

4-[5-(4-fluoro-phenyl)-2R-(1S-hydroxy-hydroxycarbamoyl-methyl)-pentanoyl]-2S-i-butyl-piperazine-1-carboxylic acid tert-butyl ester; and

6-(4-ethoxy-phenyl)-2S-methoxy-3R-[4-(2-fluoro-phenyl)-piperazine-1carbonyl]-hexanoic acid hydroxyamide.

22. (Previously Presented) A pharmaceutical composition comprising a compound as claimed in Claim 1, together with a pharmaceutically acceptable carrier.

23. (Canceled)

24. (Previously Presented) A method of treatment or prophylaxis of ~~diseases or conditions responsive to inhibition of MMP-12 and/or MMP-9~~ arthritis in mammals, which method comprises administering to the mammal an effective amount of a compound as claimed in Claim 1.

25. (Canceled)

26. (Previously Presented) A method as claimed in claim 24 wherein the ~~disease or condition is bone resorption, tumour growth or invasion by secondary metastases;~~ arthritis is selected from rheumatoid arthritis, septic arthritis, osteoarthritis, ~~periodontitis, gingivitis, corneal ulceration, cardiac hypertrophy, acute respiratory distress syndrome, neuroinflammatory disorders, e.g. multiple sclerosis; restenosis; emphysemia; fibrotic disease e.g. fibrosis post radiotherapy, kerotid scarring, liver fibrosis and cystic fibrosis; chronic obstructive pulmonary disease; bronchitis; asthma; autoimmune disease; transplant rejection (e.g. graft versus host disease); cystic fibrosis; psoriasis;~~ or psoriatic arthritis; ~~degenerative cartilage loss; inflammatory gastric conditions, e.g. Crohn's disease, inflammatory bowel disease, and ulcerative colitis; atopic dermatitis, epidermolysis bullosa; epidermic ulceration; a neuropathy or nephropathy e.g. interstitial nephritis, glomerulonephriris or renal failure; ocular inflammation; liver cirrhosis, Sjoegren's syndrome; or an inflammatory condition of the nervous system~~.

Claims 27-30 (Canceled)